Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached page is captioned "Version With Markings to Show Changes Made." Deletions are bracketed and additions are underlined. Reconsideration of the application as amended and based on the arguments set forth herein below is respectfully requested.

Response to the First Rejection of Claims Under

35 U.S.C. §112, First Paragraph

Claims 1-5 and 7 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which is not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Specifically, the Examiner contends that the description of B lymphocytes exhibiting a transmembrane signal transduction response of a degree not observed in conventional B lymphocytes encompasses numerous B lymphocytes that are not described in the subject application. The Examiner also suggests that the claims should include a description of a distinct structure and associated physiological function of the B lymphocytes, such as B lymphocytes that overexpress CD19. Official Action, page 4, lines 17-19. Applicant respectfully traverses this rejection and submits the following comments.

Initially, claim 2 has been canceled. Thus, applicant respectfully submits that the rejection under 35 U.S.C. § 112, first paragraph, is rendered partially moot by the cancellation of claim 2.

Claim 1 has been amended to recite "an animal overexpressing CD19 and having antibody-producing cells that display disrupted peripheral tolerance." Applicant respectfully submits that the language "an animal overexpressing CD19 and having antibody producing cells" recites a distinct structure, and that the language "that display disrupted peripheral tolerance" recites a physiological function associated with that structure, as disclosed in the subject application as originally filed.

Based on the foregoing arguments, claim 1 is believed to adequately describe the present invention in accordance with 35 U.S.C. § 112, first paragraph. Claim 2 has been canceled. Claims 3-5 and 7 depend from claim 1, and based on this dependency, claims 3-5 and 7 are also believed to comply with the written description requirement of 35 U.S.C. § 112, first paragraph. Thus, applicant respectfully requests that the rejection of claims 1, 3-5 and 7 under 35 U.S.C. § 112, first paragraph, be withdrawn. Applicant also respectfully requests allowance of claims 1, 3-5 and 7.

Response to the Second Rejection of Claims Under

35 U.S.C. §112, First Paragraph

Claims 1-5 and 7 are also rejected under 35 U.S.C. §112, first paragraph, as failing to teach how to use the invention. The Examiner's reasons for this rejection are set forth at pages 6-9 of the Official Action. Summarily, the Examiner asserts that the specification teaches how to use B lymphocytes that overexpress CD19, but does not teach methods employing all B lymphocytes exhibiting an unconventional

transmembrane signal transduction response. Specifically, the Examiner contends that the application fails to adequately describe the numerous B lymphocytes encompassed by the claims. Official Action, page 7, lines 13-15.

In addition, the Examiner asserts that the disclosure of transgenic mice overexpressing CD19 cannot be extrapolated to include other transgenic animals because a skilled artisan cannot envision the detailed structure of B lymphocytes possessing the recited characteristics Official Action, page 7, lines 17-20. In particular, the Examiner points to the unpredictability of transgenic expression in different species. Official Action, pages 8-9. Applicant respectfully traverses this rejection based on the arguments set forth herein below.

Initially, claim 2 has been canceled. Thus, applicant respectfully submits that the rejection under 35 U.S.C. § 112, first paragraph, is rendered partially moot by the cancellation of claim 2.

Claim 1 has been amended to recite "an animal overexpressing CD19 and having antibody-producing cells that display disrupted peripheral tolerance." Thus, claim 1 pertains to a subset of B lymphocytes exhibiting a transmembrane signal transduction response of a degree not observed in conventional B lymphocytes. Specifically, amended claim 1 recites those B lymphocytes overexpressing CD19 and that display disrupted peripheral tolerance, as disclosed in the subject application.

With regard to the alleged unpredictability of transgenic methods, applicant respectfully submits that opinion; however, the cited documents were published 1-11 years prior to the filing of the subject application and are not believed to be representative of the state of the art at the time of filing.

Applicant respectfully submits that techniques for preparing transgenic animals were known in the art at the time of filing the subject patent application. In support thereof, representative techniques for generating transgenic animals are described in U.S. Patent No. 5,489,742 (transgenic rats); U.S. Patent No. 5,573,933 (transgenic pigs); 5,162,215 (transgenic avian species) U.S. Patent No. 5,741,957 (transgenic bovine species), U.S. Patent No. 5,792,902 (transgenic rabbits), and U.S. Patent No. 5,907,080 (transgenic goats), copies of which are attached.

Applicant further submits that the subject invention is not limited to methods employing a transgenic animal. For example, subjects displaying multiple sclerosis also show overexpression of CD19, as is known in the art. *See e.g.*, Bongioanni et al (1996) *J Neurol Science* 139:71-77. Applicant respectfully submits that an inventive element of the present application pertains to improved antibody production observed in animals overexpressing CD19. As disclosed in the subject application, a preferred but not exclusive embodiment of the present invention employs a transgenic animals overexpressing CD19. Levels of CD19 expression can be assayed using standard molecular biology techniques to identify or confirm that an animal overexpresses CD19 and thus is suitable for use in the methods of the present invention.

Based on the foregoing arguments, applicant believes that claims 1, 3-5 and 7 meet the enablement requirement of 35 U.S.C. § 112, first paragraph. Claim 2 has been cancelled. Claims 3-5 and 7 depend from claim 1, and based on this dependency, claims 3-5 and 7 are also believed to comply with the enablement requirement of 35 U.S.C. § 112, first paragraph. Thus, applicant respectfully requests that the rejection of claims 1, 3-5 and 7 under 35 U.S.C. § 112, first

paragraph, be withdrawn. Applicant also respectfully requests allowance of claims 1, 3-5 and 7.

CONCLUSIONS

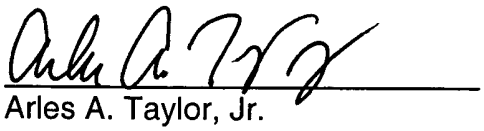
In light of the above amendments and remarks, applicant submits that the subject patent application is in condition for allowance and such allowance is earnestly solicited.

If any small matter should remain outstanding after the Patent Examiner has had an opportunity to review the above Remarks, the Patent Examiner is respectfully requested to telephone the undersigned patent attorney in order to place the application in condition for allowance.

Although it is believed that no fee is due, the Commissioner is hereby authorized to charge any deficiencies of payment associated with the filing of this correspondence to Deposit Account No. **50-0426**.

Respectfully submitted,

JENKINS & WILSON, P.A.

Date: 10/24/2002 By: 

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

Claim 1 has been amended as follows:

1. (Twice Amended) A method for production of a monoclonal antibody to an antigen comprising:

(a) immunizing an animal overexpressing CD19 and having antibody-producing cells that display disrupted peripheral tolerance, [having B lymphocytes exhibiting a transmembrane signal transduction response of a degree not observed in conventional B lymphocytes], with an [said] antigen to permit said B lymphocytes to produce antibodies to said antigen;

(b) removing at least a portion of said antibody-producing cells from said animal;

(c) forming a hybridoma by fusing one of said B lymphocytes with an immortalizing cell wherein said hybridoma is capable of producing a monoclonal antibody to said antigen;

(d) propagating said hybridoma; and

(e) harvesting the monoclonal antibodies produced by said hybridoma.